# [All-cause mortality and survival in adults with 22q11.2 deletion syndrome.](https://www.ncbi.nlm.nih.gov/pubmed/30948858)

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**Take Home Points:**

* 22q11.2 deletion is the most common microdeletion syndrome and frequently encountered in patients with congenital heart disease – particularly conotruncal anomalies.
* Little is known about the longer-term survival of adult patients with 22q11.2 deletion syndrome.
* This was a retrospective review of 309 adults with 22q11.2 deletion syndrome and their 1014 unaffected parents/siblings.
* 22q11.2 deletion syndrome is associated with almost 9x independent risk of mortality compared to siblings without 22q11.2. (HR 8.86, 95% CI 2.87-27.37).
* Of the patients with 22q11.2 deletion there were 31 deaths at a median age of 46 years (range 18 -69 years).
* As one would expect, patients with ‘major ‘congenital heart disease had shorter survival than patients with non-major congenital heart disease.
* Probability of survival of patients with 22q11.2 and major congenital heart disease to live to age 40 and 50 years was approximately 82% and 63% vs 98% and 85% in patients without major congenital heart disease.



***Commentary from Dr. Damien Cullington (Liverpool, UK), section editor of ACHD Journal Watch:*** 22q11.2 deletion syndrome is thought to be inherited in 1 in 3000-4000 live births. Penetrance is very high but with wide phenotypic variability. There has been little investigation of the importance of 22q11.2 deletion in adults and this retrospective analysis sought to address what implications 22q11.2 has on survival in affected subjects compared to their siblings/parents.

**Patient demographics and outcomes**

Patients were identified from a specialty clinic for adults with 22q11.2, via referrals or screening of patients with congenital heart disease (CHD). Over four fifths of patients were Caucasian (n=260) and 52% (n=161) were women. 469 siblings and 545 parents without 22q11.2 were enrolled as comparators. ‘Major’ congenital heart disease (n=112) was defined as persons with at least moderate complexity CHD, most of whom had tetralogy of Fallot (n=80). 309 subjects >17 years old with 22q11.2 deletion agreed to participate – of these, just over a third (n=112) had ‘major’ CHD.

The primary outcome measure was all cause mortality. Medical records and postmortem studies were reviewed to establish cause of death. Follow up was for a relatively modest median period of 5.3 years (range 0.1-21.5 years). During follow up, 31 subjects with 22q11.2 deletion died at a median age of 46 years old (range 18-69 years) - mostly resulting from cardiac causes (n=22) (**Table 1**). In comparison, 6 subjects without 22q11.2 deletion died at a median age of 58 years old (range 24-83 years old).

Controlling for other significant co-variables (such as the presence of major CHD), there was an independent relationship between survival and presence of a 22q11.2 microdeletion (**Table 2).**  Subjects with 22q11.2 deletion had worse survival if they had ‘major’ CHD versus ‘non-major’ CHD (**Figure 1**).

**Table 1** Cause of death in 31 adults with 22q11.2 deletion syndrome and relationship to CHD complexity ****

**Table 2** Cox regression models for mortality risk in 309 adults with 22q11.2 deletion syndrome



**Figure 1**



**Conclusions**

This analysis is reported to be the largest study of adult patients with 22q11.2 deletion to assess longer term survival compared to siblings and their parents not known to have 22q11.2 deletion. 22q11.2 microdeletion is a significant, independent risk factor for shorter survival. There is interesting, emerging data that rare, biallelic pathogenic variants of the *TANGO2* gene within the 22q11.2 region may be associated with a more ‘malignant’ phenotype connected to sudden cardiac death and unexpected death in epilepsy. As one may expect, subjects with a 22q11.2 deletion plus major CHD had worse survival than those with milder forms of CHD.

Larger cohorts with longer term follow up is required to gather a more complete picture of the significance of 22q11.2 deletion syndrome in relation to survival. Compared to earlier analyses, median age of death in patients with 22q11.2 appears to be increasing which is reassuring.